SYNTHESIS OF 2,2-DIMETHYLBENZOXAZEPINONES BY THE SCHMIDT REACTION OF 2,2-DIMETHYL-4-CHROMANONES[1]

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Abstract ——— 2,3-Dihydro-2,2-dimethyl-1,4-benzoxazepin-5(4H)-ones and 2,3-dihydro-2,2-dimethyl-1,5-benzoxazepin-4(5H)-ones have been synthesized by the Schmidt reaction of 2,2-dimethyl-4-chromanones. 2,2-Dimethylbenzoxazepinthiones have been prepared by the reaction of 2,2-dimethylbenzoxazepinones with Lawesson's Reagent.

INTRODUCTION

Schmidt reaction of 4-chromanones variously substituted in the aromatic moiety was studied by several research groups. Huckle *et al.*[2] and Sidhu *et al.*[3] found that 4-chromanones unsubstituted in the *peri*-position gave 2,3-dihydro-1,4-benzoxazepin-5(4H)-ones as major product in relatively good yield and the appropriate 1,5-isomers could not be isolated. Evans and Lockhart[4] reported that 5-methyl-4-chromanones afforded 2,3-dihydro-1,5-benzoxazepin-4(5H)-ones as single product but in poor yield (3-5 %). The same reaction of flavanones (2-aryl-4-chromanones) yielded 2-aryl-2,3-dihydro-1,4-benzoxazepin-5(4H)-ones as major products as well.[5-7] While the isoflavanone (3-phenyl-4-chromanone) gave the appropriate 1,4- and 1,5-benzoxazepine isomers in 2:1 ratio under the same reaction conditions.[8] To our knowledge, the conversion of 2,2-dimethyl-4-chromanones into 2,2-

dimethylbenzoxazepinones has not yet been investigated. Since relatively few representatives of 2,2-dimethylbenzoxazepine derivatives have hitherto been described,[9-11] it seemed expedient to study the Schmidt reaction of the 2,2-dimethyl-4-chromanones.

RESULTS AND DISCUSSION

Recently we synthesized a large series of 2,2-diemthyl-4-chromanones with different substituents in the aromatic moiety.[12,13] This variety of the substitution pattern made possible the study of the influence of the substituents on the formation of the possible benzoxazepinone isomers. In case 2,2-dimethyl-4-chromanones (1 - 31) were allowed to react with hydrazoic acid in acetic acid solution 2,3-dihydro-2,2-dimethyl-1,4-benzoxazepin-5(4H)-ones (40 - 70) were obtained as major product. Thin-layer chromatographic (tlc) investigation of the reaction mixture revealed the presence of small amount of various by-products but none of them could be isolated by careful column chromatography.

1 - 31 40 - 70

1, 40: $R^1 = R^2 = R^3 = R^4 = H$

2, 41: $R^1 = R^2 = R^4 = H$, $R^3 = CH_3O$

3, 42: $R^1 = R^4 = H$, $R^2 = R^3 = CH_3O$

4, 43: $R^1 = R^2 = H$, $R^3 = CH_3O$, $R^4 = CH_3$

5, 44: $R^1 = R^2 = R^4 = H$, $R^3 = C_6H_5CH_2O$

6, 45: $R^1 = R^2 = R^4 = H$, $R^3 = 2\text{-}Cl\text{-}C_6H_4CH_2O$

7, 46: $R^1 = R^2 = R^4 = H$, $R^3 = 4\text{-}Cl\text{-}C_6H_4CH_2O$

8, 47: $R^1 = R^2 = R^4 = H$, $R^3 = 4\text{-Br-}C_6H_4CH_2O$

9, 48: $R^1 = R^2 = R^4 = H$, $R^3 = 4\text{-}NO_2\text{-}C_6H_4CH_2O$

10, 49: $R^1 = R^4 = H$, $R^2 = OH$, $R^3 = C_6H_5CH_2O$

11, 50: $R^1 = R^2 = R^4 = H$, $R^3 = HO_2CCH_2O$

12, 51: $R^1 = R^2 = H$, $R^3 = HO_2CCH_2O$, $R^4 = CH_3$

13, 52: $R^1 = R^2 = R^4 = H$, $R^3 = C_2H_5O_2CCH_2O$

14, 53: $R^1 = R^2 = H$, $R^3 = C_2H_5O_2CCH_2O$, $R^4 = CH_3$

15, 54: $R^1 = R^2 = R^4 = H$, $R^3 = NCCH_2O$

16, 55: $R^1 = R^2 = R^4 = H$, $R^3 = H_2NCOCH_2O$

17, 56: $R^1 = R^2 = R^4 = H$, $R^3 = C_6H_5NHCOCH_2O$

18, 57: $R^1 = R^2 = H$, $R^3 = C_6H_5NHCOCH_2O$, $R^4 = CH_3$

19, 58: $R^1 = R^2 = R^4 = H$, $R^3 = 2\text{-}CH_3\text{-}C_6H_4NHCOCH_2O$

20, 59: $R^1 = R^2 = R^4 = H$, $R^3 = 2\text{-Cl-}C_6H_4NHCOCH_2O$

21, 60: $R^1 = R^2 = R^4 = H$, $R^3 = 3\text{-Cl-}C_6H_4NHCOCH_2O$

22, 61: $R^1 = R^2 = R^4 = H$, $R^3 = 2\text{-Br-}C_6H_4NHCOCH_2O$

23, 62: $R^1 = R^2 = R^4 = H$, $R^3 = 3\text{-Br-}C_6H_4NHCOCH_2O$

24, 63: $R^1 = R^2 = R^4 = H$, $R^3 = 2,6\text{-}Cl_2\text{-}C_6H_3NHCOCH_2O$

25, 64: $R^1 = R^2 = R^4 = H$, $R^3 = 2\text{-}CH_3$, $6\text{-}C_2H_5\text{-}C_6H_3NHCOCH_2O$

26, 65: $R^1 = R^4 = H$, $R^2 = 4\text{-}CH_3\text{-}C_6H_4NHCOCH_2O$, $R^3 = C_6H_5CH_2O$

27, 66: $R^1 = R^2 = R^4 = H$, $R^3 = CH_3SO_3$

28, 67: $R^1 = R^2 = R^4 = H$, $R^3 = C_6H_5SO_3$

29, 68: $R^1 = R^2 = R^4 = H$, $R^3 = 4\text{-}CH_3\text{-}C_6H_4SO_3$

30, 69: $R^1 = R^4 = H$, $R^2 = R^3 = C_6H_5SO_3$

31, 70: $R^1 = R^4 = H$, $R^2 = R^3 = 4\text{-}CH_3\text{-}C_6H_4SO_3$

While the same reaction of 2,2,5-trimethyl-4-chromanones (32 - 38) and the 5,7-dimethoxy-2,2-dimethyl-4-chromanone (39) afforded 2,3-dihydro-2,2-dimethyl-1,5-benzoxazepin-4(5H)-ones (71 - 78) as sole isolable product.

32 - 39 71 - 78

32, 71: $R^1 = CH_3$, $R^2 = R^4 = H$, $R^3 = CH_3O$

33, 72: $R^1 = CH_3$, $R^2 = R^4 = H$, $R^3 = C_6H_5CH_2O$

34, 73: $R^1 = CH_3$, $R^2 = R^4 = H$, $R^3 = 2\text{-}Cl\text{-}C_6H_4CH_2O$

35, 74: $R^1 = CH_3$, $R^2 = R^4 = H$, $R^3 = 4\text{-}Br\text{-}C_6H_4CH_2O$

36, 75: $R^1 = CH_3$, $R^2 = R^4 = H$, $R^3 = 4\text{-}NO_2\text{-}C_6H_4CH_2O$

37, 76: $R^1 = CH_3$, $R^2 = R^4 = H$, $R^3 = C_6H_5NHCOCH_2O$

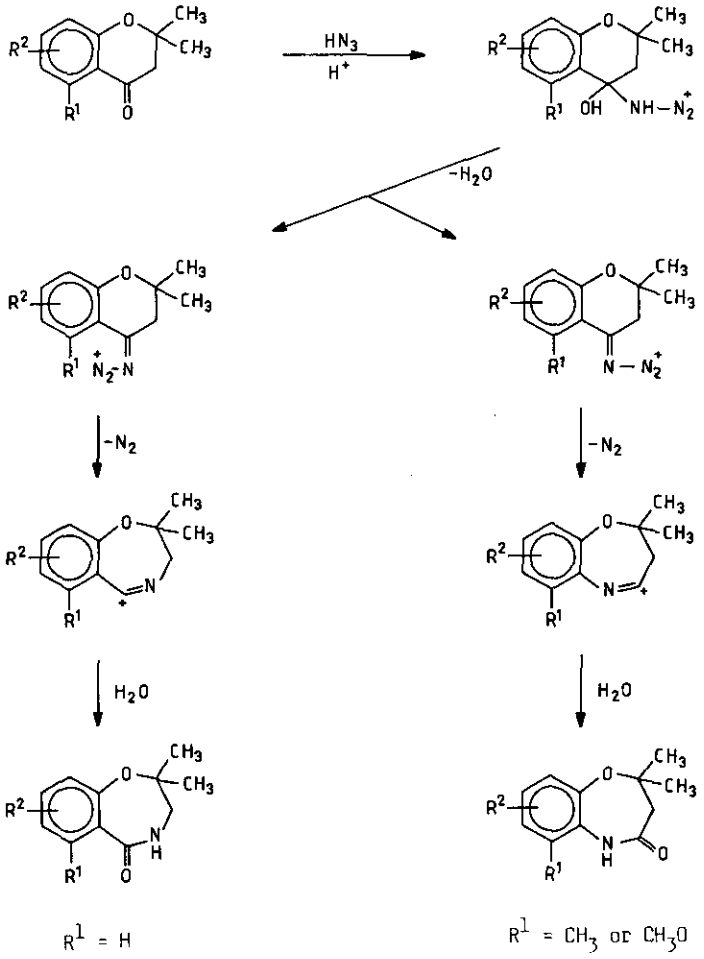
38, 77: $R^1 = CH_3$, $R^2 = R^4 = H$, $R^3 = CH_3SO_3$

39, 78: $R^1 = R^3 = CH_3O$, $R^2 = R^4 = H$

Structures of all the compounds prepared were elucidated by microanalysis and by ^{1}H-Nmr spectroscopy and the relevant data are summarized in Tables 1 and 2. In the case of compounds (40 - 70) a doublet CH_2 signal characteristic for the 2,3-dihydro-2,2-dimethyl-1,4-benzoxazepin-5(4H)-one structure was found at about 3.00 - 3.10 ppm (J = approx. 6 Hz) and the NH signal appeared as a broad singlet (br s) or a pseudotriplet. The NH signal was extinguished and the CH_2 doublet became a singlet on addition of D_2O to the solution. In the ^{1}H-Nmr spectra of substances (71 - 78) a sharp CH_2 singlet was assigned at approx. 2.40 - 2.50 ppm and no other change than the disappearance of the NH signal was observed if D_2O was added which unequivocally proved the 2,3-dihydro-2,2-dimethyl-1,5-benzoxazepin-4(5H)-one character of these molecules.

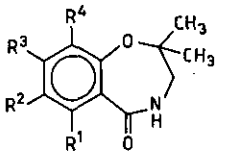
On the basis of our experimental results it can be concluded that if a hy-

drogen is in the peri-position of the 2,2-dimethyl-4-chromanone the major product of the Schmidt reaction is a 2,3-dihydro-2,2-dimethyl-1,4-benzoxazepin-5(4H)-one irrespective of the type and position of the substituent of the aromatic moiety of the chromanone skeleton. However, when a methyl or methoxy group is in the peri-position the major product is a 2,3-dihydro-2,2-dimethyl-1,5-benzoxazepin-4(5H)-one in each case. These findings are in accordance with those found in the case of 4-chromanones[2-4] and can be explained by the mechanism of the Schmidt reaction of ketones.

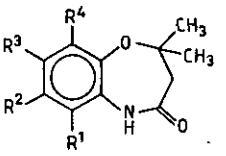


According to the explanation of Smith and Antoniades[14] a deciseve factor is the stereochemistry of the iminodiazonium ion since the migration occurs anti to the diazonium nitrogens. If this rule holds in our case, the steric effect of the peri-positioned methyl or methoxy group hinders the formation of iminodiazonium ion giving rise to alkyl migration leading to 1,4-benzoxazepinones. For this reason, in such cases 1,5-benzoxazepinones formed by aryl migration are obtained. Electronic effect of the substituent in the peri-position should not be excluded but the evaluation of such an effect would require the investigation of the influence of e.g. electron-withdrawing substituents as well. For the present studies such compounds were not available for us.

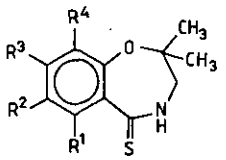
Amide → thioamide conversion of the 1,4- and 1,5-benzoxazepinones prepared has also been studied. 2,3-Dihydro-2,2-dimethyl-1,4-benzoxazepin-5(4H)-ones (41 - 46) and 2,3-dihydro-2,2-dimethyl-1,5-benzoxazepin-4(5H)-ones (71 - 73 and 75) were allowed to react with Lawesson's Reagent in hot anhydrous toluene to afford thioamides (79 - 80). This thiation method proved to be convenient in the case of these benzoxazepinones as well.



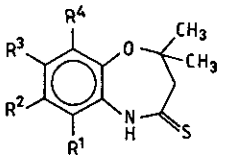
41 - 46



71 - 73, 75



79 - 84



85 - 88

79: $R^1 = R^2 = R^4 = H$, $R^3 = CH_3O$

80: $R^1 = R^4 = H$, $R^2 = R^3 = CH_3O$

81: $R^1 = R^2 = H$, $R^3 = CH_3O$, $R^4 = CH_3$

82: $R^1 = R^2 = R^4 = H$, $R^3 = C_6H_5CH_2O$

83: $R^1 = R^2 = R^4 = H$, $R^3 = 2\text{-}Cl\text{-}C_6H_4CH_2O$

84: $R^1 = R^2 = R^4 = H$, $R^3 = 4\text{-}Cl\text{-}C_6H_4CH_2O$

85: $R^1 = CH_3$, $R^2 = R^4 = H$, $R^3 = CH_3O$

86: $R^1 = CH_3$, $R^2 = R^4 = H$, $R^3 = C_6H_5CH_2O$

87: $R^1 = CH_3$, $R^2 = R^4 = H$, $R^3 = 2\text{-}Cl\text{-}C_6H_4CH_2O$

88: $R^1 = CH_3$, $R^2 = R^4 = H$, $R^3 = 4\text{-}NO_2\text{-}C_6H_4CH_2O$

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. ^{1}H-Nmr spectra in $CDCl_3$ (A) and DMSO-d_6 (B) (TMS as int. ref.) were recorded with a Bruker WP 200 SY spectrometer at 200 MHz. Tlc was performed on a Kieselgel 60 F_{254} (Merck) layer using hexane-acetone (7:3 v/v) as eluant. Starting materials (1 - 10 and 17 - 39) were prepared as described by us.[12,13]

7-Carboxymethoxy-2,2-dimethyl-4-chromanone 11

A mixture of compound 13 (5.6 g, 20 mmol), 2 N NaOH (10.0 ml, 20 mmol), and ethanol (100 ml) was refluxed for 15 min, cooled to room temperature and acidified with dilute HCl, the precipitate was filtered off and washed with water to obtain 4.3 g (79.6%) of 11, mp 192 - 193 °C. Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.63. Found C, 62.54; H, 5.58. ^{1}H-Nmr: δ 1.46 (s, 6H), 2.64 (s, 2H), 4.68 (s, 2H), 6.34 - 7.74 (m, 3 aromat.).

Table 1. Physical constants and analytical data of compounds (40 - 88)

Compound	mp °C	Yield %	Overall formula	Calculated N%	Calculated S%	Found N%	Found S%
40	151-152	57.0	$C_{11}H_{13}NO_2$	7.32	-	7.29	-
41	138-139	47.3	$C_{12}H_{15}NO_3$	6.32	-	6.44	-
42	175-176	54.0	$C_{13}H_{17}NO_4$	5.57	-	5.51	-
43	244-245	55.3	$C_{13}H_{17}NO_3$	5.95	-	5.89	-
44	174-175	70.7	$C_{18}H_{19}NO_3$	4.71	-	4.77	-
45	161-162	51.5	$C_{18}H_{18}NO_3Cl$	4.22	-	4.23	-
46	146-147	60.6	$C_{18}H_{18}NO_3Cl$	4.22	-	4.18	-
47	154-155	47.8	$C_{18}H_{18}NO_3Br$	3.72	-	3.70	-
48	187-188	90.9	$C_{18}H_{18}N_2O_5$	8.18	-	8.11	-
49	273-274	41.5	$C_{18}H_{19}NO_4$	4.47	-	4.40	-
50	231-232	64.1	$C_{13}H_{15}NO_5$	5.28	-	5.23	-
51	261-262	75.0	$C_{14}H_{17}NO_5$	5.01	-	4.94	-
52	121-122	70.9	$C_{15}H_{19}NO_5$	4.77	-	4.87	-
53	270-271	72.7	$C_{16}H_{21}NO_5$	4.55	-	4.49	-
54	167-168	44.7	$C_{13}H_{14}N_2O_3$	11.37	-	11.72	-
55	205-206	51.3	$C_{13}H_{16}N_2O_4$	10.59	-	10.46	-
56	147-148	46.1	$C_{19}H_{20}N_2O_4$	8.22	-	8.27	-
57	225-226	61.5	$C_{20}H_{22}N_2O_4$	7.90	-	7.72	-
58	206-205	53.8	$C_{20}H_{22}N_2O_4$	7.90	-	7.91	-
59	224-225	61.4	$C_{19}H_{19}N_2O_4Cl$	7.47	-	7.51	-
60	133-134	86.5	$C_{19}H_{19}N_2O_4Cl$	7.47	-	7.34	-
61	227-228	61.9	$C_{19}H_{19}N_2O_4Br$	6.68	-	6.75	-
62	139-140	60.9	$C_{19}H_{19}N_2O_4Br$	6.68	-	6.63	-
63	194-195	48.4	$C_{19}H_{18}N_2O_4Cl$	6.84	-	6.77	-
64	203-204	51.6	$C_{23}H_{28}N_2O_5$	6.78	-	6.75	-
65	201-202	38.8	$C_{27}H_{28}N_2O_5$	6.08	-	6.07	-

Table 1 continued

Compound	mp °C	Yield %	Overall formula	Calculated N%	Calculated S%	Found N%	Found S%
66	160-161	52.6	$C_{12}H_{15}NO_5S$	4.91	-	4.96	-
67	164-165	34.6	$C_{17}H_{17}NO_5S$	4.03	-	3.97	-
68	176-177	47.2	$C_{18}H_{19}NO_5S$	3.87	-	3.85	-
69	193-194	42.0	$C_{23}H_{21}NO_8S_2$	2.78	-	2.79	-
70	191-192	45.1	$C_{25}H_{25}NO_8S_2$	2.63	-	2.62	-
71	261-262	48.9	$C_{13}H_{17}NO_3$	5.95	-	5.96	-
72	259-260	58.5	$C_{19}H_{21}NO_3$	4.49	-	4.60	-
73	226-227	57.9	$C_{19}H_{20}NO_3Cl$	4.05	-	4.10	-
74	254-255	43.6	$C_{19}H_{20}NO_3Br$	3.58	-	3.62	-
75	282-283	46.3	$C_{19}H_{20}N_2O_5$	7.85	-	7.86	-
76	283-284	56.9	$C_{20}H_{22}N_2O_4$	7.90	-	7.88	-
77	250-251	46.7	$C_{13}H_{17}NO_5S$	4.68	-	4.69	-
78	217-218	54.1	$C_{13}H_{17}NO_4$	5.57	-	5.37	-
79	202-203	66.0	$C_{12}H_{15}NO_2S$	-	13.48	-	13.56
80	217-218	90.2	$C_{13}H_{17}NO_3S$	-	11.97	-	11.75
81	256-257	75.4	$C_{13}H_{17}NO_3S$	-	12.73	-	12.79
82	237-238	57.6	$C_{18}H_{19}NO_2S$	-	10.21	-	10.18
83	257-258	86.5	$C_{18}H_{18}NO_2ClS$	-	9.20	-	9.18
84	210-211	76.9	$C_{18}H_{18}NO_2ClS$	-	9.20	-	9.26
85	206-207	75.4	$C_{13}H_{17}NO_2S$	-	12.73	-	12.67
86	191-192	67.3	$C_{19}H_{21}NO_2S$	-	9.77	-	9.75
87	171-172	76.9	$C_{19}H_{20}NO_2ClS$	-	8.84	-	8.73
88	193-194	74.9	$C_{19}H_{20}N_2O_4S$	-	8.59	-	6.63

7-Carboxymethoxy-2,2,8-trimethyl-4-chromanone 12

A mixture of substance 14 (5.8 g, 20 mmol), 2 N NaOH (10.0 ml, 20 mmol),

and ethanol (100 ml) was allowed to react as described for compound (11) to yield 5.2 g (92.2%) of 12, mp 245 - 247 °C. Anal. Calcd for $C_{14}H_{16}O_5$: C, 63.62; H, 6.10. Found: C, 63.84; H, 6.17. ^{1}H-Nmr δ 1.44 (s, 6H), 2.04 (s, 3H), 2.72 (s, 2H), 4.64 (s, 2H), 6.57 (1H, d, J=8.37 Hz), 7.54 (1H, d, J=8.37 Hz).

2,2-Dimethyl-7-ethoxycarbonylmethoxy-4-chromanone 13

A mixture of 2,2-dimethyl-7-hydroxy-4-chromanone (3.0 g, 15 mmol), ethyl bromoacetate (2.5 ml, 22 mmol), anhydrous potassium carbonate (5.0 g, 36 mmol), sodium iodide (0.1 g, 0.6 mmol), and anhydrous acetone (100 ml) was refluxed for 6 h, the solid material was filtered off, the solvent was evaporated and the residue was crystallized from ethanol to afford 3.4 g (87.1%) of 13, mp 101 - 102 °C. Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.74; H, 6.47. Found: C, 64.90; H, 6.44. ^{1}H-Nmr δ 1.30 (3H, t, J=7.5 Hz), 1.46 (s, 6H), 2.68 (s, 2H), 4.29 (2H, q, J=7.5 Hz), 4.65 (s, 2H), 6.36 - 7.87 (m, 3 aromat.).

7-Ethoxycarbonylmethoxy-2,2,8-trimethyl-4-chromanone 14

7-Hydroxy-2,2,8-trimethyl-4-chromanone (6.0 g, 29 mmol) was allowed to react with ethyl bromoacetate (5.0 ml, 44 mmol) as described for compound (13) to obtain 6.7 g (77.0%) of 14, mp 98 - 99 °C. Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.73; H, 6.89. Found: C, 65.74; H, 6.77. ^{1}H-Nmr: δ 1.32 (3H, t, J=7.4 Hz), 1.45 (s, 6H), 2.29 (s, 3H), 2.64 (s, 2H), 4.30 (2H, q, J=7.4 Hz), 4.67 (s, 2H), 6.36 (1H, d, J=8.40 Hz), 7.64 (1H, d, J=8.40 Hz).

7-Cyanomethoxy-2,2-dimethyl-4-chromanone 15

2,2-Dimethyl-7-hydroxy-4-chromanone (6.0 g, 30 mmol) and chloroacetonitrile (4.0 ml, 63 mmol) were allowed to react as described for substance (13) to yield 5.2 g (72.2%) of 15, mp 114 - 115 °C. Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.53; H, 5.62. Found: C, 67.66; H, 5.74 ^{1}H-Nmr: δ 1.50 (s, 6H), 2.70 (s, 2H), 4.52 (s, 2H), 6.41 - 7.88 (m, 3 aromat.).

Table 2. ^{1}H-Nmr spectral properties of compounds 40-88

Compound	Solvent	δ (ppm)
40	A	1.40 (s, 6H), 3.09 (2H, d, J=6.04 Hz), 6.96-7.78 (m, 4 aromat.), 8.34 (br s, NH)
41	A	1.41 (s, 6H), 3.12 (2H, d, J=6.02 Hz), 3.84 (s, 3H), 6.50-7.72 (m, 3 aromat.), 7.76 (br s, NH)
42	A	1.39 (s, 6H), 3.12 (2H, d, J=5.95 Hz), 3.88 (s, 6H), 6.52 (s, 1H), 7.26 (s, 1H), 7.58 (br s, NH)
43	A	1.30 (s, 6H), 2.04 (s, 3H), 2.90 (2H, d, J=5.86 Hz), 3.84 (s, 3H), 6.81 (1H, d, J=8.79 Hz), 7.37 (1H, d, J=8.51 Hz), 8.21 (br s, NH)
44	A	1.38 (s, 6H), 3.08 (2H, d, J=6.06 Hz), 5.06 (s, 2H), 6.56-7.72 (m, 8 aromat.), 7.58 (br s, NH)
45	A	1.41 (s, 6H), 3.10 (2H, d, J=6.06 Hz), 5.17 (s, 2H), 6.58-7.72 (m, 7 aromat.), 7.78 (br s, NH)
46	A	1.36 (s, 6H), 3.11 (2H, d, J=5.90 Hz), 5.04 (s, 2H), 6.56-7.75 (m, 7 aromat.), 6.97 (br s, NH)
47	A	1.40 (s, 6H), 3.11 (2H, d, J=6.04 Hz), 5.02 (s, 2H), 6.53-7.75 (m, 7 aromat.), 6.97 (br s, NH)
48	A	1.29 (s, 6H), 2.98 (2H, d, J=6.07 Hz), 5.33 (s, 2H), 6.64-8.27 (m, 7 aromat.), 8.31 (br s, NH)
49	B	1.24 (s, 6H), 2.89 (2H, d, J=6.02 Hz), 5.12 (s, 2H), 6.57 (s, 1H), 6.97 (s, 1H), 7.33-7.49 (m, 5 aromat.), 8.16 (br s, NH), 12.26 (s, OH)
50	B	1.28 (s, 6H), 2.96 (2H, d, J=5.98 Hz), 3.42 (br s, CO_2H), 4.24 (s, 2H), 6.42-7.50 (m, 3 aromat.), 8.26 (br s, NH)
51	B	1.31 (s, 6H), 2.10 (s, 3H), 2.97 (2H, d, J=6.02 Hz, 3.40 (br s, CO_2H), 6.70 (1H, d, J=8.48 Hz), 7.37 (1H, d, J=8.50 Hz), 8.30 (br s, NH)

Table 2 continued

Compound	Solvent	δ (ppm)
52	A	1.30 (3H, t, J=7.4 Hz), 1.34 (s, 6H), 3.13 (2H, d, J=6.04 Hz), 4.38 (2H, q, J=7.4 Hz), 6.49-7.71 (m, 3 aromat.), 7.23 (br s, NH)
53	A	1.30 (3H, t, J=7.50 Hz), 1.34 (s, 6H), 2.19 (s, 3H), 3.12 (2H, d, J=6.04 Hz), 4.29 (2H, q, J=7.50 Hz), 4.67 (s, 2H), 6.46 (1H, d, J=8.60 Hz), 7.54 (1H, d, J=8.60 Hz), 7.87 (br s, NH)
54	A	1.38 (s, 6H), 3.11 (2H, d, J=6.06 Hz), 4.80 (s, 2H), 6.58-7.80 (m, 3 aromat.), 7.35 (br s, NH)
55	B	1.29 (s, 6H), 2.96 (2H, d, J=6.02 Hz), 4.49 (s, 2H), 6.50-7.52 (m, 3 aromat.), 7.64 (br s, NH_2), 8.26 (br s, NH)
56	A	1.42 (s, 6H), 3.13 (2H, d, J=6.04 Hz), 4.64 (s, 2H), 6.58-7.82 (m, 8 aromat.), 6.72 (br s, NH), 8.18 (s, NH)
57	B	1.33 (s, 6H), 2.18 (s, 3H), 2.95 (2H, d, J=6.02 Hz), 4.78 (s, 2H), 6.74-7.68 (m, 7 aromat.), 8.27 (br s, NH), 10.11 (s, NH)
58	A	1.42 (s, 6H), 2.26 (s, 3H), 3.14 (2H, d, J=6.10 Hz), 4.70 (s, 2H), 6.57-7.94 (m, 7 aromat.), 6.87 (br s, NH), 8.17 (s, NH)
59	A	1.41 (s, 6H), 3.14 (2H, d, J=6.06 Hz), 4.68 (s, 2H), 6.60-8.44 (m, 7 aromat.), 7.21 (br s, NH), 8.95 (s, NH)
60	B	1.28 (s, 6H), 2.97 (2H, d, J=6.05 Hz), 4.69 (s, 2H), 6.57-7.83 (m, 7 aromat.), 8.28 (br s, NH), 10.30 (s, NH)
61	A	1.42 (s, 6H), 3.13 (2H, d, J=6.04 Hz), 4.68 (s, 2H), 6.59-8.43 (m, 7 aromat.), 6.97 (br s, NH), 8.98 (s, NH)
62	B	1.30 (s, 6H), 2.93 (2H, d, J=6.08 Hz), 4.78 (s, 2H), 6.53-7.97 (m, 7 aromat.), 8.28 (br s, NH), 10.30 (s, NH)
63	A	1.41 (s, 6H), 3.14 (2H, d, J=6.06 Hz), 4.75 (s, 2H), 6.52-7.80 (m, 6 aromat.), 6.97 (br s, NH), 8.07 (s, NH)

Table 2 continued

Compound	Solvent	δ (ppm)
64	A	1.17 (3H, t, J=7.60 Hz), 1.41 (s, 6H), 2.25 (s, 3H), 2.60 (2H, q, J=7.60 Hz), 3.12 (2H, d, J=6.05 Hz), 4.78 (s, 2H), 6.63-7.31 (m, 6 aromat.), 7.60 (brs, NH), 8.22 (s, NH)
65	A	1.41 (s, 6H), 2.32 (s, 3H), 3.14 (2H, d, J=6.04 Hz), 4.63 (s, 2H), 5.15 (s, 2H), 6.67-7.49 (m, 11 aromat.), 7.59 (br s, NH), 8.67 (s, NH)
66	A	1.41 (s, 6H), 3.14 (2H, d, 6.04 Hz), 3.18 (s, 3H), 6.93-7.82 (m, 3 aromat.), 7.07 (br s, NH)
67	A	1.32 (s, 6H), 3.07 (2H, d, J=6.08 Hz), 6.68-7.88 (m, 8 aromat.), NH signal is overlapped
68	A	1.37 (s, 6H), 2.45 (s, 3H), 3.06 (2H, d, J=6.06 Hz), 6.68-7.72 (m, 7 aromat.), NH signal is overlapped
69	A	1.41 (s, 6H), 3.15 (2H, d, J=6.01 Hz), 6.99 (s, 1H), 7.35 (br s, NH), 7.43-7.84 (m, 11 aromat.)
70	A	1.40 (s, 6H), 2.42 (s, 3H), 2.48 (s, 3H), 3.14 (2H, d, J=6.02 Hz), 6.97-7.72 (m, 10 aromat.), 7.08 (br s, NH)
71	A	1.50 (s, 6H), 2.26 (s, 3H), 2.48 (s, 2H), 3.70 (s, 3H), 6.50-6.58 (m, 2 aromat.), 6.96 (s, NH)
72	A	1.50 (s, 6H), 2.26 (s, 3H), 2.48 (s, 2H), 5.01 (s, 2H), 6.77 (s, NH), 6.54-7.40 (m, 7 aromat.)
73	A	1.48 (s, 6H), 2.27 (s, 3H), 2.48 (s, 2H), 5.64 (s, 2H), 7.17 (s, NH), 6.58-7.56 (m, 6 aromat.)
74	B	1.39 (s, 6H), 2.20 (s, 3H), 2.30 (s, 2H), 5.06 (s, 2H), 6.50-7.61 (m, 6 aromat.), 9.04 (s, NH)
75	B	1.36 (s, 6H), 2.21 (s, 3H), 2.30 (s, 2H), 5.26 (s, 2H), 6.53-8.29 (m, 6 aromat.), 9.07 (s, NH)

Table 2 continued

Compound	Solvent	δ (ppm)
76	A	1.50 (s, 3H), 1.59 (s, 3H), 2.30 (s, 3H), 2.50 (s, 2H), 4.60 (s, 2H), 6.78 (s, NH), 6.60-7.62 (m, 7 aromat.), 8.20 (s, NH)
77	A	1.52 (s, 6H), 2.32 (s, 3H), 2.51 (s, 2H), 3.19 (s, 3H), 6.87-6.99 (m, 2 aromat.), 7.26 (s, NH)
78	A	1.43 (s, 6H), 2.98 (s, 2H), 3.80 (s, 3H), 3.89 (s, 3H), 6.08-6.14 (m, 2 aromat.), 11.47 (s, NH)
79	A	1.43 (s, 6H), 3.21 (2H, d, J=6.04 Hz), 3.83 (s, 3H), 6.46-8.04 (m, 3 aromat.), 9.59 (br s, NH)
80	A	1.43 (s, 6H), 3.22 (2H, d, J=6.06 Hz), 3.90 (s, 3H), 3.94 (s, 3H), 6.49 (s, 1H), 7.51 (s, 1H), 9.73 (br s, NH)
81	B	1.34 (s, 6H), 2.07 (s, 3H), 3.08 (2H, d, J=6.02 Hz), 3.85 (s, 3H), 6.85 (1H, d, J=8.47 Hz), 7.68 (1H, d, J=8.47 Hz), 10.72 (s, NH)
82	A	1.41 (s, 6H), 3.21 (2H, d, J=6.07 Hz), 5.10 (s, 2H), 6.54-8.03 (m, 8 aromat.), 8.70 (br s, NH)
83	B	1.36 (s, 6H), 3.12 (2H, d, J=6.06 Hz), 5.26 (s, 2H), 6.60-7.81 (m, 7 aromat.), 10.77 (br s, NH)
84	A	1.42 (s, 6H), 3.21 (2H, d, J=6.02), 5.08 (s, 2H), 6.50-8.02 (m, 7 aromat.), 9.10 (br s, NH)
85	A	1.56 (s, 6H), 2.34 (s, 3H), 2.98 (s, 2H), 3.80 (s, 3H), 6.48-6.61 (m, 2 aromat.), 9.13 (s, NH)
86	A	1.51 (s, 6H), 2.30 (s, 3H), 2.94 (s, 2H), 5.01 (s, 2H), 6.53-7.40 (m, 7 aromat.), 9.11 (s, NH)
87	A	1.54 (s, 6H), 2.31 (s, 3H), 2.97 (s, 2H), 5.15 (s, 2H), 6.56-7.58 (m, 6 aromat.), 9.02 (s, NH)

Table 2 continued

Compound	Solvent	δ (ppm)
88	A	1.55 (s, 6H), 2.38 (s, 3H), 2.97 (s, 2H), 5.17 (s, 2H), 6.50-8.30 (m, 6 aromat.), 9.08 (s, NH)

7-Aminocarbonylmethoxy-2,2-dimethyl-4-chromanone 16

2,2-Dimethyl-7-hydroxy-4-chromanone (3.0 g, 15 mmol) and chloroacetamide (2.5 g, 26 mmol) were allowed to react as described for compound (13) to afford 2.4 g (63.1%) of 16, mp 142 - 143 °C. Anal. Calcd for $C_{13}H_{14}NO_4$: C, 62.65; H, 6.02. Found: C, 62.62; H, 6.03. ^{1}H-Nmr: δ 1.47 (s, 6H), 2.70 (s, 2H), 4.79 (s, 2H), 6.48 - 7.89 (m, 3 aromat.).

General procedure for the Schmidt reaction of 2,2-dimethyl-4-chromanones 1 - 39

Concentrated sulfuric acid (3.0 ml, 56 mmol) was added portionwise to the stirred and cooled mixture of 2,2-dimethyl-4-chromanone (1 - 39: 10 mmol), sodium azide (30 mmol), and glacial acetic acid (20.0 ml). The mixtures was stirred for further 3 h at 50 °C and then poured into water. The solution was neutralized with 5% $NaHCO_3$ and extracted with chloroform. The organic phase was washed with brine, dried with $CaCl_2$, and the solvent was evaporated. The residue was crystallized from methanol to give compounds (40 - 78) (Tables 1 and 2).

General procedure for the preparation of the 2,3-dihydro-2,2-dimethylbenzoxazepinthiones 79 - 88

A mixture of 2,3-dihydro-2,2-dimethylbenzoxazepinone (41 - 46, 71 - 73, and 75; 0.5 g, 1.5 mmol), Lawesson's Reagent (0.6 g, 1.5 mmol), and anhydrous toluene (25.0 ml) was refluxed for 3 h, then the solvent was evaporated under reduced pressure and the residue was crystallized from methanol to afford substances (79 - 88) (Tables 1 and 2).

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